

Complex Formation Between Polyelectrolytes and Ionic Surfactants

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The interaction between polyelectrolyte and ionic surfactant is of great importance in different areas of chemistry and biology. In this paper we present a theory of polyelectrolyte ionic-surfactant solutions. The new theory successfully explains the cooperative transition observed experimentally, in which the condensed counterions are replaced by ionic-surfactants. The transition is found to occur at surfactant densities much lower than those for a similar transition in non-ionic polymer-surfactant solutions. Possible application of DNA surfactant complex formation to polynucleotide delivery systems is also mentioned.

INTRODUCTION

Solutions containing polyelectrolytes remain an outstanding challenge to physical-chemistry. Due to the long-ranged nature of the Coulomb force our understanding of this class of polymers is still quite rudimentary. This situation can be compared to the one that existed in electrochemistry of the turn of the century, before Debye and Hückel (DH) presented their, now famous, theory of strong electrolytes [1]. The fundamental question that must be addressed by any successful theory of polyelectrolytes concerns with the role played by the counterions. In this respect, the traditional theories of liquid state are not of great help, since most of the approaches based on resolution of integral equations come to a dead-end when the numerical schemes used to tackle these difficult problems fail to converge. The scaling theories, which have been so successful in elucidating the properties of nonionic polymers [2] have, so far, proven futile in the face of large number of length scales relevant for polyelectrolyte solutions. What seems to be lacking is a mean-field theory of polyelectrolytes similar to the one created by Debye and Hückel for simple electrolytes, and Flory for non-ionic polymers. In our previous work we have attempted to construct such a mean-field theory for one special class of polymer solutions, the rigid polyelectrolytes [3,4]. The constraint of rigidity allowed us to study the effects of electrostatic interactions decoupled from that of conformational structure of polyions. The theory has proven to be successful in elucidating various thermodynamic properties of rigid polyelectrolytes in the presence, or in the absence, of monovalent salt. In this letter we shall present a theory of rigid polyelectrolyte and ionic-surfactant solutions.

The interaction between polymers and surfactants is of great practical importance in areas as diverse as col-

loidal stabilization, polymer solubilization, mineral flotation and flocculation, as well as various aspects of molecular biology and biochemistry [5]. In many practical applications the polymers are dissolved in some sort of polar solvent, typically water, leading to monomer ionization. This situation is very common for biological systems. For example, in an aqueous solution, the phosphate groups of a DNA molecule become ionized, giving it a net negative charge. Similarly the phospholipids, which compose the cell membrane, in aqueous environment acquire a net negative charge. The repulsion between the like-charged molecules makes the introduction of a polynucleotide sequence into a cell a formidable challenge to molecular biologists. It has been observed, however, that in the case of binding by ionic surfactant dissolved in a polyelectrolyte solution, the adsorption isotherms show a striking degree of cooperativity. This surprising phenomenon suggests that ionic surfactants or ionic lipids can be used as a “packaging” in order to deliver polynucleotides into living cells. Indeed, some recent experiments demonstrate that the cationic lipid reagents provide some of the best methods available for the gene delivery systems [6].

THE MODEL

The solution under consideration consists of anionic polyions, monovalent salt, and cationic surfactant, inside a volume V (see Fig.1). It is important to remember that the overall system is charge neutral, what implies that the negative charge of polyions and the positive charge of surfactants is counterbalanced by an appropriate number of counterions (univalent cations), and coions (univalent anions), respectively. Furthermore, to simplify the analysis we shall assume that all of the counterions are identical,

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whether they are derived from polyions or from disassociation of monovalent salt. A similar approximation will be made in the case of coions.

In order to study the interaction between an ionic surfactant and a polyelectrolyte we resort to the simplest possible model. The rigid polyions, of density ρ_p , are represented by cylinders of length L and diameter a_p . Each polyion has a charge $-Zq$, uniformly distributed along the length of the cylinder. The spacing between each charged group is $b \equiv L/Z$. The cationic surfactants, of density ρ_s , are modeled as flexible chains of n_s monomers each, with the head group carrying a charge $+q$. For simplicity we shall assume that each monomer is a sphere of diameter a_c . The density of counterions (cations) is $\rho_{count} = Z\rho_p + \rho_{salt}$, while the density of coions (anions) is $\rho_{coion} = \rho_{salt} + \rho_s$. Both the coions and the counterions will be modeled as hard spheres of diameter a_c and charge $\pm q$ located at their centers. The solvent (water) will be represented by a uniform medium of dielectric constant D .

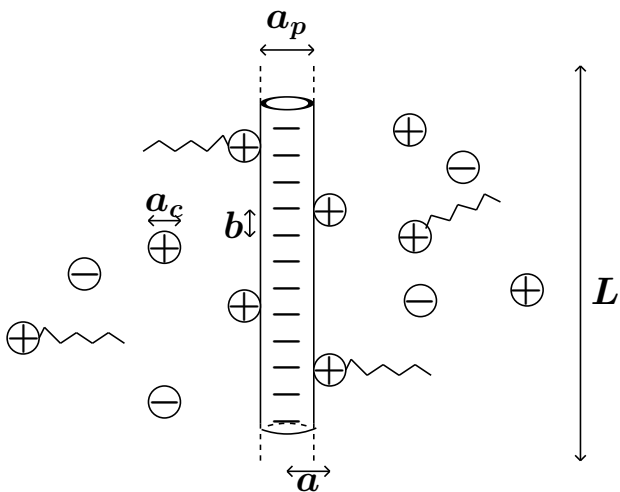


FIG. 1. A polyion of (cylindric) diameter a_p and length $L \gg a$ surrounded by spherical counterions and coions of diameter a_c , and flexible surfactant molecules. The charge spacing on the polyion is $b \equiv L/Z$, and the radius of the exclusion cylinder is $a \equiv (a_p + a_c)/2$.

The strong electrostatic interaction between the polyions, the counterions, and the surfactants leads to formation of clusters each made of **one** polyion, n_B counterions, and m_B surfactants. In what follows we shall neglect the effects of polydispersity in cluster sizes, since it can be shown not to significantly affect the final results [3,4]. The counterion and surfactant association with the polyions reduces the number of free entities. Charge conservation implies

$$\rho_+ = \rho_{count} - n_B \rho_p, \quad (1)$$

$$\rho_- = \rho_{coion}, \quad (2)$$

$$\rho_s^+ = \rho_s - m_B \rho_p, \quad (3)$$

where ρ_+ is the density of free counterions, ρ_- is the density of coions, and ρ_s^+ is the density of free amphiphiles.

THE THEORY

The main task of the theory is to determine the characteristic cluster size, i.e., to find the values of n_B and m_B . In order to achieve this goal the appropriate Helmholtz free energy has to be constructed and minimized. The free energy can be decomposed into an electrostatic and an entropic contributions. The electrostatic contribution arises due to the *polyion-counterion-surfactant*, the *polyion-polyion*, and the *counterion-coion-surfactant* interactions. The entropic part is the result of mixing of various species [3,4].

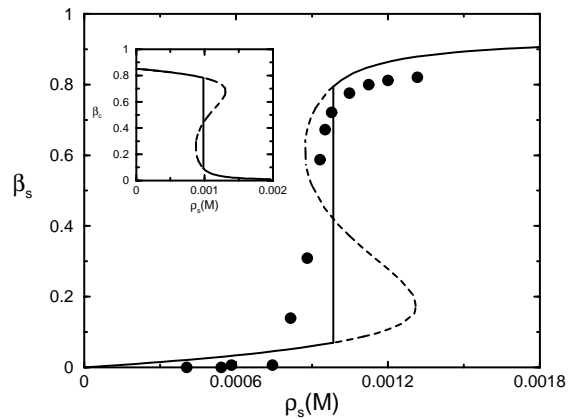


FIG. 2. The DNA-DoTAB binding isotherms, $\chi = -4k_B T$, $Z = 440$, and $\xi = 4.17$ for DNA at room temperature. The diameters of the polyions and the counterions are 27 \AA and 7.04 \AA , respectively. The size of surfactant molecule is $n_s = 13$. The concentrations of DNA and of added salt are $2 \times 10^{-6} \text{ M}$ and 18 mM , respectively. Note that at the transition the condensed counterions are replaced by the ionic surfactants. The transition is found to be of the first order with the vertical line locating the point at which two local minima of the free energy become equal. The solid circles are the experimental data from Ref.[13].

The *polyion-counterion-surfactant* and the *counterion-coion-surfactant* contributions can be obtained in the spirit of DH theory [1,3,4]. As a counterion or a surfactant associates with a polyion it neutralizes one of its charged groups. Hence, the effective charge per unit length of a cluster, made of n_B bound counterions and m_B bound surfactants, is $\sigma_{cl} = -q(Z - n_B - m_B)/L$. Let us fix one such cluster and ask what is the potential that it feels due to the electrostatic interactions with the other

entities. In order to answer this question it is necessary to solve the Poisson equation, $\nabla^2 \Phi^{(cl)} = -4\pi\rho_q/D$. Due to the hard core exclusion, for $r < a \equiv (a_p + a_c)/2$ the charge distribution can be approximated as,

$$\rho_q = \frac{\sigma_{cl}}{2\pi} \frac{\delta(r)}{r}. \quad (4)$$

For $r > a$, in the spirit of DH theory, we shall assume that

$$\rho_q = -(Z - n_B - m_B)q\rho_p + q\rho_+ e^{-\beta q\Phi^{(cl)}(r)} - q\rho_- e^{+\beta q\Phi^{(cl)}(r)} + q\rho_s^+ e^{-\beta q\Phi^{(cl)}(r)}, \quad (5)$$

where $\beta = 1/(k_B T)$. Upon linearization, the Poisson-Boltzmann equation can be easily solved to yield [3,4]

$$\Phi_{in}^{(cl)} = -\frac{2\sigma_{cl}}{D} \ln(r/a) + \frac{2\sigma_{cl}}{D} \frac{K_0(\kappa a)}{\kappa a K_1(\kappa a)}, \quad r < a, \quad (6)$$

$$\Phi_{out}^{(cl)} = \frac{2\sigma_{cl}}{D} \frac{K_0(\kappa r)}{\kappa a K_1(\kappa a)}, \quad r > a, \quad (7)$$

where $(\kappa a)^2 \equiv 4\pi\rho_1^*/T^*$, $\rho_1 \equiv \rho_+ + \rho_- + \rho_s^+$, and the reduced density and temperature are respectively $\rho_i^* = \rho_i a^3$ and $T^* = D a k_B T / q^2$, while $K_n(x)$ are the n-order modified Bessel functions of second kind. It is important to recall that the linearization of the Poisson-Boltzmann equation is justified by the renormalization of polyion charge through formation of clusters [3,4,7,9].

In terms of this potential, the electrostatic energy of a cluster is

$$U^{(cl)} = \frac{1}{2} \int \rho_q \Delta\Phi^{(cl)} d^3r, \quad (8)$$

with $\Delta\Phi^{(cl)} = \Phi_{in}^{(cl)} + (2\sigma_{cl}/D) \ln(r/a)$, for $r < a$; $\Delta\Phi^{(cl)} = \Phi_{out}^{(cl)}$, for $r > a$. That is, we subtract the logarithmic potential produced by a line of charge, since it will only contribute to the self energy of a cluster. The electrostatic *free energy density*, $f \equiv -F/V$, for the polyion-counterion-surfactant interaction is obtained through the Debye charging process, where all the particles are charged from 0 to their final charge [1,8],

$$\begin{aligned} \beta f^{pcs} &= -\rho_p \int_0^1 \frac{2\beta U^{(cl)}(\lambda q n_B, \lambda q m_B, \lambda q Z)}{\lambda} d\lambda \\ &= -\rho_p (Z - n_B - m_B)^2 \frac{(a/L)}{T^*(\kappa a)^2} \times \\ &\quad \times \left\{ -2 \ln[\kappa a K_1(\kappa a)] + I(\kappa a) - \frac{(\kappa a)^2}{2} \right\}, \quad (9) \end{aligned}$$

where

$$I(\kappa a) \equiv \int_0^{\kappa a} dx \frac{x K_0^2(x)}{K_1^2(x)}. \quad (10)$$

The electrostatic correlational free energy arising from the interactions between the free counterions, coions, and free surfactants is obtained using the usual Debye-Hückel theory [1,9],

$$\beta f^{ccs} = \frac{1}{4\pi a_c^3} \left[\ln(1 + \kappa a_c) - \kappa a_c + \frac{(\kappa a_c)^2}{2} \right]. \quad (11)$$

For sufficiently large separations the effective electrostatic potential of interaction between two clusters separated by a distance r is [4,10]

$$V_{pp}(r) = \frac{2\pi\sigma_{cl}^2}{D\kappa \sin\theta} \frac{\exp(-\kappa r)}{(\kappa a)^2 K_1^2(\kappa a)}, \quad (12)$$

where θ is the angle between two complexes. The short-ranged nature of the effective cluster-cluster interaction allows us to write its contribution to the free energy as a second virial term, averaged over the relative angle sustained by two macromolecules,

$$\begin{aligned} \beta f^{pp} &= -\frac{1}{2} \rho_p^2 \left\langle \int d^3r \beta V_{pp}(r) \right\rangle_\theta \\ &= -\frac{2\pi}{T^*} \frac{\exp(-2\kappa a)}{(\kappa a)^4 K_1^2(\kappa a) a^3} (Z - n_B - m_B)^2 \rho_p^{*2}. \quad (13) \end{aligned}$$

The entropic (mixing) free energy is obtained using the ideas derived from the Flory theory [11]. In general $f^{ent} = \sum_i f_i^{ent}$, where f_i^{ent} is the entropic contribution of each specie i . For free counterions and coions,

$$\beta f_\pm^{ent} = \rho_\pm - \rho_\pm \ln \phi_\pm, \quad (14)$$

where $\phi_\pm = (\pi\rho_\pm^*/6)(a_c/a)^3$ are the volume fractions occupied by free counterions and coions. For flexible surfactant chains the entropic free energy is [11]

$$\beta f_s^{ent} = \rho_s^+ - \rho_s^+ \ln[\phi_s^+/n_s], \quad (15)$$

where the volume fraction of surfactant is

$$\phi_s^+ = n_s \frac{\pi\rho_s^{*+}}{6} \left(\frac{a_c}{a}\right)^3. \quad (16)$$

Finally, for complexes made of one rigid polyion, n_B counterions, and m_B surfactants, we find

$$\beta f_{cl}^{ent}(\rho_p) = \rho_p - \rho_p \ln \left[\frac{\phi_{cl}(Z + n_B + m_B)}{(Z + n_s m_B + n_B) \zeta_{cl}} \right], \quad (17)$$

with

$$\phi_{cl} = \pi\rho_p^* \left[\frac{1}{4(a/L)} \left(\frac{a_p}{a}\right)^2 + \frac{1}{6} (n_s m_B + n_B) \left(\frac{a_c}{a}\right)^3 \right], \quad (18)$$

and, ζ_{cl} , the internal partition function of a (n_B, m_B) -complex,

$$\zeta_{cl} = \text{Tre}^{-\beta H[\sigma_c(t), \sigma_s(t)]}. \quad (19)$$

The trace is taken over all possible configurations of n_B counterions and m_B surfactants associated to a polyion. The occupation variables, $\sigma_c(t)$ and $\sigma_s(t)$, are such that $\sigma_c(t) = 1$ if the monomer t of the polyion is occupied by a condensed counterion, and $\sigma_c(t) = 0$ if no counterion is associated at t . The occupation variable, $\sigma_s(t)$, behaves in the same way, but for an association with surfactants. The Hamiltonian can be written as

$$H = \frac{q^2}{2} \sum_{t_1 \neq t_2} \frac{[-1 + \sigma_c(t_1) + \sigma_s(t_1)][-1 + \sigma_c(t_2) + \sigma_s(t_2)]}{D|r(t_1) - r(t_2)|} + \frac{\chi}{2} \sum_{\langle t_1 \neq t_2 \rangle} \sigma_s(t_1)\sigma_s(t_2). \quad (20)$$

An implicit constraint is that each monomer can have either a counterion or a surfactant associated, but not both. We have also made a simplifying assumption that the only effect of counterion or surfactant association is a local renormalization of a monomer charge. Note that the first term of the Hamiltonian couples all the sites, since it is due to the long-ranged Coulomb potential. The second sum runs only over the nearest neighbors, and is related to the hydrophobic interaction of the hydrocarbon tails. The configurations in which agglomerates of surfactant molecules form are energetically favored, i.e. the hydrophobicity parameter is negative, $\chi < 0$.

Even this, seemingly simple one-dimensional subproblem, is impossible to solve exactly due to the long-ranged nature of the Coulomb force. We will, therefore, resort to a mean-field bound given by the Gibbs-Bogoliubov-Feynman inequality. Defining $x \equiv n_B/Z$, and $y \equiv m_B/Z$ we find [4]

$$\begin{aligned} \ln \zeta_{cl} \approx & -\xi S(x^2 + 2xy + y^2 - 2x - 2y) + \\ & -\beta\chi y^2(Z-1) + \\ & -Z(1-x-y)\ln(1-x-y) + \\ & -Z(x\ln x + y\ln y), \end{aligned} \quad (21)$$

where $S \equiv Z[\psi(Z) - \psi(1)] - Z + 1$, $\psi(x)$ is the digamma function, and $\xi \equiv \beta q^2/(Db)$ is the Manning parameter [12]. In our previous study we have numerically checked that this, indeed, is a good approximation [4].

Minimization of the total free energy, $f = f^{ent} + f^{pcs} + f^{ccs} + f^{pp}$, with respect to n_B and m_B allows us to determine the characteristic number of bound counterions, n_B^* , and of bound surfactants, m_B^* . We shall compare the predictions of our theory with the experimental measurements on DNA dodecyltrimethylammonium bromide (DoTAB) system [13,14]. The DoTAB is a cationic surfactant with an alkyl chain of twelve carbons. We can estimate the value of the hydrophobicity parameter, χ , as follows. Consider a micell or a monolayer composed of DoTABs. The hydrophobic energy required to take an alkyl chain of twelve carbons from bulk hydrocarbon to water is measured to be approximately $20k_B T$ [15]. We can interpret this energy as derived from the favorable interaction between the adjacent surfactants. Since each surfactant inside a micell or a monolayer has five or six nearest neighbors, we can estimate $\chi \approx -4k_B T$. Clearly this is only a rough estimate but it should be sufficient to explore the ramifications of the new theory.

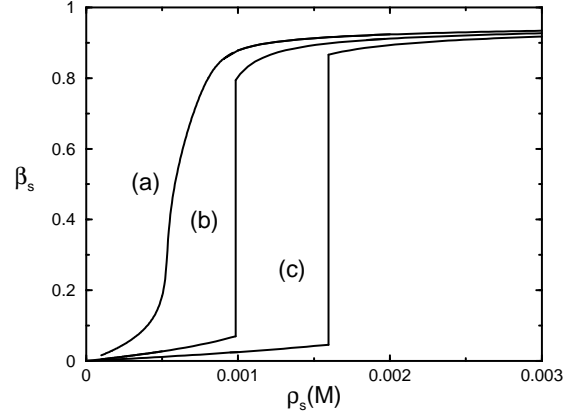


FIG. 3. The DNA-DoTAB binding isotherms for various concentrations of added salt: (a) 5 mM, (b) 18 mM, (c) 40 mM. The other experimental parameters are the same as in Fig.2. Note the change in the order of transition as it passes from continuous to discontinuous with an increase in the density of monovalent salt.

In discussions of adsorption it is traditional to define binding fractions, $\beta_c \equiv n_B^*/Z$ and $\beta_s \equiv m_B^*/Z$. In Fig.2 we present the binding isotherms of DNA with dodecyltrimethylammonium bromide, and compare it with the experimental data of [13]. It is evident that the agreement is quite good, without any fitting parameters! We note, however, that at densities of monovalent salt used in experiment, our theory predicts a first-order transition, while the experimental data is more consistent with a second-order transition. In Fig.3 we demonstrate that as the concentration of monovalent salt is lowered the transition becomes continuous.

CONCLUSION

We have presented a mean-field theory of polyelectrolyte-ionic-surfactant solutions. Although quite simple, our theory manages to capture the essential physics of the problem. The most nontrivial aspect of polyelectrolyte-ionic-surfactant complex formation is that it occurs at extremely low densities, about a factor of twenty lower than the critical micell concentration (CMC) of pure amphiphile. This should be compared to the interaction of nonionic polymer with surfactant, in which case the binding transition happens at densities close to the CMC. Our theory explains this dichotomy in terms of strong electrostatic interactions which, in ad-

dition to hydrophobic forces, govern the polyelectrolyte-surfactant complex formation.

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